

## REMARKS

Claims 1, 2, 31, 34, 36, 38, and 43, as amended, and claims 4-10, 22-25, 28, 32, 33, 35, 37, 39-42, and 44 are pending in the instant application. Support for the amendments to the claims can be found in the specification at, for example, page 10, lines 3-6; page 14, lines 22-29; page 31, lines 12-15; page 46, lines 19-21; page 46, line 27 to page 47, line 2; and page 66, lines 1-6. No new matter has been added as a result of the above-described amendments. The rejections set forth in the Office Action have been overcome by amendment or are traversed by argument below.

**1. Rejections of claims 31, 34, 36, 38, and 43 under 35 U.S.C. § 112, second paragraph**

The Office Action asserts a rejection of claims 31, 34, 36, 38, and 43 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention.

The Action first asserts that claims 31 and 43 are vague and indefinite because they are incomplete kit claims. The Examiner suggests that this rejection can be overcome by amending claims 31 and 43 to insert the phrase “a first container containing” after the term “comprising.”

Applicants thank the Examiner for her helpful suggestion regarding the amendment of claims 31 and 43, and note that these claims have been amended to insert the phrase “a first container having” after the term “comprising.” Support for this amendment can be found in the specification at, for example, page 66, lines 1-6. Withdrawal of this ground of rejection is therefore respectfully solicited.

The Action next asserts that claims 34, 36, and 38 are vague and indefinite for reciting an sTNFR polypeptide, or a pharmaceutical composition comprising an sTNFR polypeptide, that is encoded by a polynucleotide comprising a nucleotide sequence that hybridizes to the complement of any of the nucleotide sequences recited in those claims. Specifically, the Action states that the term “hybridizes” is indefinite because the various hybridization and wash conditions described on pages 46-47 of the specification are merely exemplary. The Examiner suggests that this rejection can be overcome by amending claims 34, 36, and 38 to recite specific hybridization and wash conditions described in the specification.

Applicants thank the Examiner for her helpful suggestion regarding the amendment of claims

34, 36, and 38, and note that these claims have been amended so that they encompass a polynucleotide comprising a nucleotide sequence that hybridizes to the complement of any of the nucleotide sequences recited in those claims at 45°C in a hybridization buffer comprising 4x SSC and 0.1% SDS. Support for this amendment can be found in the specification at, for example, page 46, line 27 to page 47, line 2. Withdrawal of this ground of rejection is therefore respectfully solicited.

The Action next asserts that claims 34-39 are vague and indefinite for reciting the phrase “portion[s] thereof,” because there is no definition of the size or activity of the recited polypeptide fragments. The Examiner suggests that this rejection can be overcome by amending claims 34-39 to recite that the polypeptide fragments bind TNF $\alpha$ .

Applicants thank the Examiner for her helpful suggestion regarding the amendment of claims 34-39, and note that the claims 35, 37, and 39 have been amended to replace the phrase “or a portion thereof” with the phrase “or a TNF inhibitory fragment thereof.” Support for this amendment can be found in the specification at, for example, page 14, lines 22-29. With regard to the recitation of the phrase “or portions thereof” in at line 10 of claim 34, line 10 of claim 36, and line 11 of claim 38, Applicants note that these claims have been amended so that they encompass a polynucleotide comprising a nucleotide sequence that is a degenerate sequence of the nucleotide sequences recited in those claims. Support for this amendment can be found in the specification at, for example, page 10, lines 3-6 and page 46, lines 19-21. Because the phrase “degenerate sequence” encompasses sequences that are either partially or fully degenerate, Applicants contend that this amendment will have no substantive effect on the proper scope of claims 34, 36, and 38. With regard to the recitation of the phrase “or a portion thereof” at line 15 of claim 34, Applicants contend that one of ordinary skill in the art would readily understand that the use of the phrase here (and similarly in claims 1 and 2 and at line 15 of claim 36 and line 17 of claim 38) refers to a portion – or fragment – of residues 111-161 of SEQ ID NO: 2, and therefore, that the recitation of this phrase here is not indefinite. Withdrawal of this ground of rejection is therefore respectfully solicited.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, second paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

**2. Rejections of claims 1, 2, 4-10, 22-25, 28, 31-34, and 36-44 under 35 U.S.C. § 112, first paragraph**

The Office Action maintains a rejection of claims 1, 2, 4-10, 22-25, 28, and 31-34 and asserts a rejection of claims 40-44 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The instant Action states that the amendment of claims 1 and 2 in Applicants' response to the Office Action mailed February 21, 2003 to recite the limitation "with at least one amino acid substitution" forms the basis of this rejection. Specifically, the Action states that because there is no limit to the number of amino acid substitutions that can be made, the claims encompass a protein that can bind TNF $\alpha$ , but have a completely different amino acid sequence.

Applicants respectfully disagree with the Action's assertion that one of ordinary skill in the art would not understand the scope of species comprising the genus of truncated sTNFR polypeptides and variants defined by claims 1 and 2, as amended in Applicants' response to the Office Action mailed February 21, 2003, and that the inventors were not in possession of the invention having said scope at the time the application was filed. Nevertheless, in an effort to expedite prosecution of the pending claims to allowance, Applicants have amended claim 1 to recite a genus of truncated sTNFR polypeptides comprising a particular fragment of the amino acid sequence of SEQ ID NO: 2, and claim 2 to recite a genus of truncated sTNFR polypeptides comprising the amino acid sequence of SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, or SEQ ID NO: 14. Applicants note that claim 1, as amended, no longer recites truncated sTNFR polypeptides comprising (a) a particular fragment of the amino acid sequence of SEQ ID NO: 2 having at least one amino acid substitution; (b) a particular fragment of the amino acid sequence of SEQ ID NO: 2 having at least one amino acid addition; or (c) a particular fragment of the amino acid sequence of SEQ ID NO: 2 having at least one internal intrasequence amino acid deletion, and that claim 2, as amended, no longer recites truncated sTNFR polypeptides comprising (a) the amino acid sequence of SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, or SEQ ID NO: 14 having at least one amino acid substitution; (b) the amino acid sequence of SEQ ID NO: 4, SEQ ID

NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, or SEQ ID NO: 14 having at least one amino acid addition; or (c) the amino acid sequence of SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, or SEQ ID NO: 14 having at least one internal intrasequence amino acid deletion. Applicants reserve the right to pursue claims directed to such truncated sTNFR polypeptide variants in a timely filed continuation or divisional application. Applicants submit that claims 1 and 2, as amended, satisfy the written description requirement of 35 U.S.C. § 112, first paragraph, and respectfully request that this ground of rejection be withdrawn.

The Office Action also asserts a rejection of claims 1, 2, 4-10, 22-25, 28, 31-34, and 40-44 under 35 U.S.C. § 112, first paragraph, because claims 1 and 2 are single means claims. Specifically, the Action states that while the claims encompass every conceivable structure (means) for achieving a stated property (result), the specification discloses at most only those means known to the Applicants.

Applicants respectfully disagree with the Action's assertion that claims 1 and 2, as amended in Applicants' response to the Office Action mailed February 21, 2003 or as amended in the instant response, are single means claims. As described above, claim 1 has been amended to recite a genus of truncated sTNFR polypeptides comprising a particular fragment of the amino acid sequence of SEQ ID NO: 2, and claim 2 has been amended to recite a genus of truncated sTNFR polypeptides comprising the amino acid sequence of SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, or SEQ ID NO: 14. Applicants contend that because claims 1 and 2, as amended, define a genus of truncated sTNFR polypeptides comprising a finite number of species, all of which share substantial sequence identity with the polypeptide comprising amino acid residues 19-103 of SEQ ID NO: 2, claims 1 and 2 do not encompass every conceivable means (any and all amino acid sequences) for achieving a stated property (presumably, TNF inhibitory activity). Withdrawal of this ground of rejection is therefore respectfully solicited.

The Office Action also asserts a rejection of claims 24, 25, and 36-39 under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention. The Action acknowledges that the specification is enabling for pharmaceutical compositions comprising the recited polypeptides that are recombinantly produced

and that are isolated from host cell or nutrient medium; however, the Action asserts that the specification does not reasonably provide enablement for pharmaceutical compositions comprising the recited polypeptides that are recombinantly produced but are not isolated from host cell or nutrient medium. Specifically, the Action states that while the claims recite that the recombinantly produced polypeptides may optionally be isolated from the host cell or nutrient, it is *not* an art accepted practice to administer a pharmaceutical composition comprising a polypeptide that has not been isolated from the recombinant cell producing it or from the nutrient medium it is produced in. The Examiner suggests that this rejection can be overcome by amending claims 24, 25, and 36-39 to delete the term “optionally.”

Applicants thank the Examiner for her helpful suggestion regarding the amendment of the claims, and note that the term “optionally” has been deleted from claims 24, 25, 37, and 39, and line 18 of claim 36 and line 22 of claim 22. Withdrawal of this ground of rejection is therefore respectfully solicited.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, first paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

### **3. Rejection of claims 1 and 2 under 35 U.S.C. § 102**

The Office Action asserts a rejection of claims 1 and 2 under 35 U.S.C. § 102(b), as being anticipated by Smith *et al.*, *Science* 248:1019-23 (1990). The Action states that Smith *et al.* disclose the TNF $\alpha$  receptor II and extracellular (soluble) domain (Figure 3). The Action also states that because claims 1 and 2 recite a truncated sTNFR polypeptide comprising any of the nucleotide sequences recited in those claims, wherein the polypeptide can have at least one amino acid substitution, and because there is no limit to the number of amino acid substitutions, the claims encompass polypeptides that can bind TNF $\alpha$ , but which have completely different amino acid sequences. The Action states, therefore, that the soluble protein disclosed by Smith *et al.* meets the limitations of the claims 1 and 2.

Applicants note that the amino acid sequence of the polypeptide described by Smith *et al.* is disclosed in GenBank Accession Nos. AAA59929, P20333, NP\_001057, and A35356, each of which

discloses an identical sequence of 461 amino acid residues. Exhibit A illustrates that the truncated sTNFR polypeptide comprising amino acid residues 1-110 of SEQ ID NO: 2, as disclosed in the instant application, shares only 33.6% (37/110) identity and 48.2% (53/110) similarity with the corresponding portion of the polypeptide disclosed by Smith *et al.*

As described in section 2 above, claim 1 has been amended to recite a genus of truncated sTNFR polypeptides comprising a particular fragment of the amino acid sequence of SEQ ID NO: 2, and claim 2 has been amended to recite a genus of truncated sTNFR polypeptides comprising the amino acid sequence of SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, or SEQ ID NO: 14. Applicants contend that because Smith *et al.* does not disclose an amino acid sequence that meets each and every limitation of the claimed invention, this reference cannot anticipate claims 1 and 2, as amended. Applicants, therefore, respectfully request that the rejection of claims 1 and 2 under 35 U.S.C. § 102(b) be withdrawn.

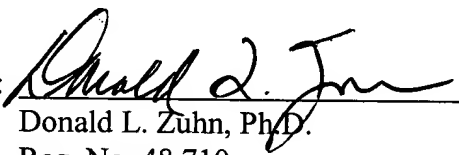
### **CONCLUSIONS**

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner O'Hara believes it to be helpful, she is invited to contact the undersigned representative by telephone at 312-913-0001.

Respectfully submitted,  
**McDonnell Boehnen Hulbert & Berghoff**

Dated: May 13, 2004

By:   
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## EXHIBIT A

SEQ ID NO: 2 (residues 1-110) vs. GenBank Accession No. AAA59929

Aligned Length = 465    Gaps = 7  
Identities = 37 (8%)    Similarities = 16 (3%)

SEQ2_1-110	1	DSVCPQGKYIHPQN	14
AAA59929	1	MAPVAVWAALAVGLELWAAHALPAQVAFTPYAPEPGSTCRLREYYD-QT	49
		* * * *	
SEQ2_1-110	15	NSICCTKCHKGTYLYNDPCPGPGQDTCRECESGSFTASENHLRHCLSC-S	63
AAA59929	50	AQMCCSKCSPGQHAKVFCTKTS-DTVCDSCEDSTYTQLWNWVPECLSCGS	98
		.***.** * * * * . . * * . *****	
SEQ2_1-110	64	KCRKEMGQVEISSCTVDRDTCVCGCRKNQYRHYWSEN-----LFQC---	103
AAA59929	99	RCSSD--QVETQACTREQNRICTCRPGWYCALSKEGECRLCAPLRKCRPG	146
		. * . *** .** .. . * * * . * . * *	
SEQ2_1-110	104	FN-----CSLCL	110
AAA59929	147	FGVARPGTETSDVVCKPCAPGTFSNTTSSTDICRPHQICNVVAIPGNASM	196
		* . * *	
SEQ2_1-110	111		110
AAA59929	197	DAVCTSTSPTRSMAPGAVHLPQPVSTRSQHTQPTPEPSTAPSTSFLPLMG	246
SEQ2_1-110	111		110
AAA59929	247	PSPPAEGSTGDFALPVGLIVGTALGLLIIGVVNCVIMTQVKKKPLCLQR	296
SEQ2_1-110	111		110
AAA59929	297	EAKVPHLPADKARGTQGPEQQHLLITAPSSSSSSLESSASALDRRAPTRN	346
SEQ2_1-110	111		110
AAA59929	347	QPQAPGVEASGAGEARASTGSSDSSPGGHGTQVNVTCIVNVCSSSDHSSQ	396
SEQ2_1-110	111		110
AAA59929	397	CSSQASSTMGDTDSSPSESPKDEQVPFSKEECAFRSQLETPETLLGSTEE	446
SEQ2_1-110	111		110
AAA59929	447	KPLPLGVDPDAGMKPS	461